

the introduction of epidemic diseases from Black Sea ports, it is most important to provide in this neighbourhood a properly equipped sanitary station on modern lines, with hospital accommodation and provision for observation of contacts and satisfactory landing places.

In regard to administration, the Report pays a tribute to the excellent sanitary work accomplished during the Inter-Allied occupation by the Inter-Allied Medical Services, and their executive British officer in the town of Constantinople as well as in the port. Regarding this administration as necessarily temporary, the Commission advises the future establishment of a port sanitary authority with an efficient organisation and an international character for the sanitary control of the Straits. It is considered also that from the point of view of practical hygiene there will be very obvious advantages in the same body when established, exercising its functions over all the ports belonging to Turkey, including the Turkish ports in the Mediterranean and Black Sea.

The annexe to the Report consists of a series of articles numbering from 57 to 165, which are proposed by the Commission in substitution for the corresponding provisions in the International Sanitary Convention of 1912. These articles are based on the revision already proposed by the Office International d'Hygiène Publique of Articles 1-56, which lay down the general requirements for all signatory countries.

ADVANCED MEDICINE: INTERNATIONAL COÖPERATION.

THE last of the present series of lectures in medicine arranged by the University of London in connexion with foreign universities was delivered last week by Prof. A. A. HIJMAN VAN DEN BERGH, of Utrecht, on the Pathology of Hæmoglobin, the chair being taken by Sir FREDERICK ANDREWES. An abstract of this lecture follows and we comment upon it editorially elsewhere.

THE PATHOLOGY OF HÆMOGLOBIN.

By PROF. A. A. HIJMAN VAN DEN BERGH.

The Paræmias.

Methæmoglobinæmia.—It is well known that a number of poisons and drugs can convert some of the normal hæmoglobin to methæmoglobin while it still circulates in the blood. Of more interest are the cases of cyanosis without pulmonary or cardiac lesions associated with pronounced enteritis and diarrhoea in which we have an autotoxic intraglobular methæmoglobinæmia. Profs. Stokvis and Talma showed that in these cases there is a methæmoglobin-producing substance in the intestines, and this has since been found to be a nitrite which has in some cases been found in the red corpuscles themselves.

Sulphæmoglobinæmia, or more conveniently sulphæmia, is liable to be confounded with methæmoglobin in cases of enterogenous cyanosis until the blood is examined. It will then be found that the abnormal pigment, unlike methæmoglobin, is not reconverted to hæmoglobin by reducing reagents, and that treatment with carbon monoxide shifts the characteristic absorption band in the red about five wave-lengths towards the violet end of the spectrum (Clarke and Wood). Most of the cases are associated with obstinate constipation, but this is not always present, and many examples of constipation show no sulphæmia. In one case of Hirschsprung's disease we have demonstrated the presence of traces of sulphuretted hydrogen in the serum on several occasions, and the addition of the boy's serum to normal blood resulted in the appearance of traces of sulphæmoglobin. The action of sulphuretted hydrogen on hæmoglobin in red corpuscles is quite slow, and any sulphuretted hydrogen in the blood is quickly destroyed by oxidation or eliminated through the lungs. Once formed,

however, sulphæmoglobin is not easily destroyed or altered and persists for a long time; if it is injected into the blood of rabbits it may be found there for several days or even weeks. Hence very small amounts of sulphuretted hydrogen may in the end produce a considerable degree of sulphæmia. Some caution is needed in making such experiments, for we have found sulphæmoglobin in the blood of 10 out of 55 normal rabbits. Feeding rabbits with sulphur causes sulphæmoglobinæmia, and small amounts are found in the blood of patients taking medicinal doses of sulphur or even such a bland preparation as apenta water. The proportion of the hæmoglobin which is altered under these circumstances is small and difficult to estimate accurately, but it appears to be from 10 to 20 per cent.

Hæmatin.

The occurrence of hæmatin in blood serum was first studied by Schumm, of Hamburg, in a case of poisoning with chromic acid. He afterwards found it not very rarely in malaria, anaerobic sepsis, eclampsia, and pernicious anæmia. I have found it very often, though not constantly, in pernicious anæmia, never in secondary anæmias, however severe, and in about half the cases of ruptured ectopic pregnancy I have examined. In small amounts and in the presence of large quantities of hæmoglobin it is difficult to demonstrate with certainty.

Bilirubin.

Not so many years ago it was rather generally believed that bilirubin originates exclusively in the liver, and it was almost heresy to believe that jaundice could develop without liver disease. It is true that Virchow had many years ago shown that crystals occurred in old hæmorrhagic foci which looked like bilirubin and were called hæmatoidin, but it is only recently that we have realised that bilirubin may be made in large quantities in other tissues than the liver. This conversion is seen especially well in cases of hæmorrhagic pleural effusion where, some 24 hours after its development, we may find a concentration of bilirubin many times greater than that in the blood at the same time. It cannot be doubted that in these cases bilirubin is formed locally in the pleural cavity itself. In the pleural cavity itself we may find as much as 100 mg. of bilirubin, while the quantity in a well-filled gall-bladder will not exceed about 40 mg. The extra-hepatic origin of bile pigment is shown by its presence in distinctly larger quantities in the splenic vein than in the splenic artery. Ernst and Szappanyos, of Budapest, have also demonstrated its production by the spleen in perfusion experiments. These observations do not, however, prove that any bile pigment is *normally* made outside the liver, nor do we know from them whether jaundice can arise without the liver taking any part in the process. Jaundice which is not plainly obstructive in origin has been explained by an increased viscosity of the bile, by the liver cells excreting bile into the blood instead of the bile capillaries, and by Eppinger's microthrombi of bile. None of these views are quite satisfactory, and it seems to me necessary to assume that the secretion and excretion of bile are carried on by different elements. I suppose that the formation of bile pigment occurs in one cell, washed by the blood; that this cell discharges its product into the blood which brings it to the second cell which excretes it into the bile capillaries. The trace of bilirubin in the blood which may be called physiological arises in this way, and the amount will be increased if the balance of activity between the secretory and excretory cells is upset. Hence in many diseases characterised by increased blood destruction—hæmolytic anæmia, pernicious anæmia, hæmorrhagic effusions—there is an increase of bilirubin in the blood. There is often, also, too much hæmatin, but the relation between the two substances is at present obscure. From the observations of Dr. Engelkes on the specific oxygen capacity of hæmoglobin in pernicious anæmia it seems that part of the decomposition may begin while the red cells are still circulating in the blood.